## <u>REMARKS</u>

The issues outstanding in the Final Rejection mailed January 6, 2009, are the rejections under 35 U.S.C. 103 of all claims. Reconsideration of these issues, in view of the following discussion, is respectfully requested.

## Rejections Under 35 U.S.C. 103

## Ishizuka taken withEguchi and Tanaka

As will be recalled, Ishizuka discloses the production of capillaries with a diameter of 100 microns, see page 372, first column, second paragraph. The authors teach that, during production of silica columns, voids develop between the silica structure and the capillary wall due to shrinkage which takes place during sol gel processing, as the gel is aged. In fact, this is a well know phenomenon, as Ishizuka indicates (noting reference 11) and, moreover, as discussed in the present specification at page 1, lines 25-35 and page 2, lines 9-20. Prior art solutions for this problem, as discussed at page 2 of the present specification, lines 22-27, addressed situations such as that of Ishizuka when relatively small diameter columns are employed.

Applicants have previously argued that it would have been apparent to one of ordinary skill in the art that the problem of shrinkage would increase with increasing column diameter. Where capillaries having small diameters such as those of Ishizuka are employed, the shrinkage rate can be kept low enough so that no voids develop, but as the column size increases, shrinkage becomes a significant issue. For example, assuming a shrinkage rate of about 10%, which is a realistic estimation, a capillary of 100 microns as in the primary reference would experience macropores of about 10 microns (note Ishizuka at page 373, second column, last paragraph) which are small enough to not be considered as void volume. However, if the diameter of the gellation mold were on the order of a millimeter, 10% shrinkage would result in voids on the average of 100 microns, which dead space would negatively impact column efficiency. It is for this reason (the use of a comparatively small column) that Ishizuka does not discuss in detail the problem of shrinkage, nor pose a solution therefore. Clearly, based on the teachings of Ishizuka alone, one of ordinary skill in the art would not expand the process to produce moldings on the

order of 0.5 to 50 millimeters, since one of ordinary skill would expect shrinkage problems from the sol gel process which would cause considerable difficulty. It is for this reason that where monolithic moldings with large diameters are produced in the prior art, they must be removed from the gellation mold and put in a tight cladding before they can be used.

Eguchi is cited, as explained at page 4 of the office action, for its teaching of the use of 3-(methacyloxy)propyltrimethoxysilane to increase the surface are of a mold wall, and allow a "stronger molecular bond between the mold and the molding." While this may be true, it does not teach one of ordinary skill in the art that the process would be effective with large scale columns in which void volume is an issue. Eguchi discloses the production of sorbent layers, that is, capillaries which are not totally filled with sorbent. Such capillaries are not monolithic, as in the primary reference (or, for that matter the claims) but are only coated. Note claim 1 of Eguchi. Consequently, the patent does not address the issue of void volumes inasmuch as, in a capillary which is only coated, there is always open space in the middle. Although patentees discuss the generation of thicker sorbent layers, at column 1, lines 63-65 and column 2, lines 17-24, it is evident that patentees do not fill the capillary completely. Moreover, the material disclosed in the patent, polymeric organic sorbents, are organic polymers which typically do not shrink. See page 1, lines 25-page 2, line 7 of the present specification. And, similarly to Ishizuka, Eguchi discloses capillaries having an internal diameter of just a few microns. As a result, both Ishizuka and Eguchi disclose materials which are not large size monolithic moldings as in the present invention, and provide no guidance to one of ordinary skill in the art suggesting that, if their process was combined, it could be further modified to produce large scale moldings, regardless of how desirable such moldings are said to be in the office action. Indeed, it cannot be overemphasized that such large scale moldings exist in the art. However, in the known production processes, they are removed from the capillary and subjected to cladding, before use. If the skilled artisans believed that the teachings of these references would be applicable to the production of large scale columns, indeed, it is submitted that the present process for producing such column would have been tried and found to work prior to the present invention. However, the common wisdom in the art, which dictated that such columns would shrink and thus must be cladded before use, clearly shows that the skilled artisan did not expect that organic silanes could

somehow be used to "glue" the column to the wall, as suggested in the office action (actually, to activate the inner wall of the mold), much less to produce a monolithic column with no void volume, regardless of any better adhesion to the walls.

It is further submitted that Tanaka does nothing to remedy the above deficiencies. It is argued, at page 4 of the office action, that Tanaka teaches monolithic porous silica columns with diameters of 7, 4.6 and 0.1 millimeters." This is correct as far as it goes, but chapter 2 of the reference, entitled "preparation method of monolithic silica columns" (see page 37, second column bridging to page 38) provides considerable illumination of the true teachings of Tanaka. In this chapter, the authors describe that the monolithic materials can be produced either in a mold, or in a capillary. The 4.6 and 7 millimeter columns are produced in molds with an internal diameter of 6 and 9 millimeters. It is thus quite evident that significant shrinking occurred. These columns are after covered with tubing, i.e., cladding as discussed above. Only the capillary columns were produced "in-column" and, tellingly, on page 38 Tanaka discloses that the silica network needs to be attached to the capillary wall and that smaller diameters (i.e., 15 microns) gave better results. As a result, the actual teaching of Tanaka is consistent with the foregoing discussion. Monolithic columns with large diameters can be produced, but shrinking requires them to be cladded. These columns are typically produced in molds, removed from the mold and covered. Only small columns where shrinking does not produce significant void volume can be produced in situ.

As a result, any combination of these references clearly would not teach one of ordinary skill in the art to produce monolithic moldings with large diameters which completely fill the gelling mold. In fact, these references emphasize the known problem of shrinking even at small diameter, so that clearly one of ordinary skill in the art would not be directed to the combination of the process features alleged to be obvious in the office action. For this reason, it is submitted that a case of *prima facie* obviousness has simply not been made by this combination of references, and withdrawal of this rejection is respectfully requested.

Claim 6 has also been rejected under 35 U.S.C. 103 over Ishizuka, Eguchi and Tanaka taken further with Zhang. Reconsideration of this rejection is also respectfully requested.

Claim 6 herein recites the further use, in the process of claim 1, of particles, fibers and/or

organoalkoxysilanes in filling of the gelling mold with monomer sol. Zhang discloses the production of "on-column frits" for capillary columns filled with particulate materials. As evident from page 16, figure 1, a very small amount of the sol-gel network is added to the particles to make them stick together. The office action notes at page 15, where tetromethoxysilane (TMOS), a common sol-gel precursor, is taught to be less flexible and mechanically stable than methyltriethoxysilane (MTES). However, nothing in this disclosure seems to teach that MTES would result in a stronger bond with a capillary wall, or less shrinkage. Moreover, the MTES in this article is essentially used as "glue". As evident from the details of the production process, for example, page 14, at the bottom bridging to page 15, the authors do not use a sol-gel process to produce a porous monolithic material. Instead, in the production of Frits a little bit of MTES is added to bond them together. This does not teach that such "glue" would be effective in the highly different environment of a sol-gel process, where monolithic are produced. This is all the more so the case considering that Zhang deals only with capillary columns having a maximum diameter of 250 microns, and regardless of any teaching therein does not, as noted above, support expansion of this teaching to the use of higher diameter columns.

In conclusion, it is accordingly respectfully submitted that, without the guidance presented in the present specification, one of ordinary skill in the art simply would not find it apparent to use the presently claimed process with any reasonable expectation of producing large columns with minimal void area. Moreover, it would not even be "obvious to try" the processes of the references with a large diameter column, inasmuch as all of the conventional wisdom in the art is that such large columns are subject to shrinkage, and must be encased before use. Withdrawal of the rejections under 35 U.S.C. 103 is therefore respectfully requested.

The claims of the application are submitted to be in condition for allowance. However, if the Examiner has any questions or comments, he is cordially invited to telephone the undersigned at the number below. The Commissioner is hereby authorized to charge any fees associated with this response or credit any overpayment to Deposit Account No. 13-3402.

Respectfully submitted,

/Harry B. Shubin/

Harry B. Shubin, Reg. No. 32,004 Attorney/Agent for Applicant(s)

MILLEN, WHITE, ZELANO & BRANIGAN, P.C. Arlington Courthouse Plaza 1, Suite 1400 2200 Clarendon Boulevard Arlington, Virginia 22201 Telephone: (703) 243-6333 Facsimile: (703) 243-6410

Attorney Docket No.: Merck-3160

Date: April 6, 2009

6 DOCKET NO.: MERCK-3160